UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/628,667	07/28/2000	David Putnam	10436-0010-999	3663

23557 7590 04/07/2005

SALIWANCHIK LLOYD & SALIWANCHIK
A PROFESSIONAL ASSOCIATION
PO BOX 142950
GAINESVILLE, FL 32614-2950

EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/628,667	PUTNAM ET AL	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *136-172* is/are pending in the application.

4a) Of the above claim(s) *137,138,142,143,148,156,157,159 and 164* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *136,139-141,144-147,149-155,158,160-163 and 165-172* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/16/04; 11/15/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection (e.g., see 1/16/04 Response). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/19/04 has been entered. Claims 136-172 are pending (e.g., see 11/15/04 and 5/19/04 Responses). Claims 137, 138, 142, 143, 148, 156, 157, 159 and 164 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species (see below i.e., ***Response to Restriction and/or Election of Species***). Therefore, claims 136, 139-141, 144-147, 149-155, 158, 160-163 and 165-172 are examined on the merits.

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

Response to Restriction and/or Election of Species

2. Applicant's election of species (e.g., see 11/15/04 Response) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election of species has also been treated as an election without traverse (MPEP § 818.03(a) and/ or 37 CFR 1.111(b)).

3. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

Priority

4. Applicant's claim for domestic priority under 35 U.S.C. 120 and 119(e) is acknowledged. However, applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The instant application is a continuation-in-part of 09/540,462, which claims priority to provisional application 60/127,755. However, 09/540,462, upon which priority is claimed, fails to provide adequate support under 35 U.S.C. § 112 for the full scope of the newly added claims. Specifically, the Examiner does not find support for the use of "robotics" (e.g., see claim 136, step (a)(4); see also claim 155). For example, although the use of "automation" is recited in 09/540,462, the application does not mention the term "robotics" nor does it provide any guidance that would reasonably lead a person of skill in the art to automation that "resembles" a human being (e.g., see Soukhanov, et al. Eds. Webster's II New Riverside University Dictionary. Boston: The Riverside Publishing Company 1988, page 1015, "**robotics** ... Study and application of the technology of robots"; "**robot** ... mechanical apparatus that resembles a human being"). If applicants believe this to be in error, applicants must disclose where in 09/540,462 support for "robotics" can be found. Thus, the claims have only been awarded the date of application, which is **July 28, 2000**.

New Rejections

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 136, 139-141, 144-147, 149-155, 158, 160-163 and 165-172 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For **claims 136 and 155**, the term "automated robotics" is vague and indefinite. For example, it is not clear how "automated" systems differ from "automated robotic" systems? For example, the Webster's Dictionary defines "robotics" to require a mechanical apparatus that "resembles a human being" (e.g., see Soukhanov, et al. Eds. Webster's II New Riverside University Dictionary. Boston: The Riverside Publishing Company 1988, page 1015, "**robotics** ... Study and application of the technology of robots"; "**robot** ... mechanical apparatus that resembles a human being"). However, the specification provides no guidance as to the nature of the resemblance (e.g., by function, shape, smell). In addition, it is not clear to what extent the robotic systems must "resemble" human beings. For example, a low degree of similarity could be required such that said robotic systems are only required to have "moving parts" (i.e., humans have moving parts). This broad interpretation of "robotics" would essentially render this term superfluous as all automated systems have moving parts. In contrast, a higher degree of similarity could be required such that a person could not tell the machine apart

from the man (e.g., same shape, color, smell, ability to talk). Here, Applicants provide no such guidance on determining the extent to which the automated robotic systems must resemble a human being nor do the provide any guidance on how such systems differ from any other automated systems. Therefore, claims 136, 155 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

B. Claims 151-154 and 167-170 recite "optimize" and/or "optimized". The term "optimize" and/or "optimized" is a relative term, which renders the claim indefinite and/or unclear. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. See also MPEP § 2173.05(b). Therefore, claims 151-154, 167-170 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

C. Claims 171-172 recite the limitation "said at least three excipients" in the first line of each claim. There is insufficient antecedent basis for this limitation in the claim. Therefore, claims 171-172 are rejected under 35 U.S.C. 112, second paragraph.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the

international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 136, 139-141, 144-147, 149-155, 158, 160-163 and 165-172 are rejected under 35 U.S.C. 102(e) as being anticipated by Levinson et al. et al. (WO 01/51919 A2).

For ***claims 136 and 155***, Levinson et al. (see entire document) disclose methods and arrays for the high-throughput formation, identification and analysis of diverse solid-forms including "formulations" of small molecule pharmaceuticals that have a "component-in-common" such as an excipients and/or a solvent (see Levinson et al., abstract; see also claims), which anticipates the claimed invention. For example, Levinson et al. disclose preparing an array of samples (e.g., see Levinson et al., claim 22, "A method of preparing an array"). Levinson further disclose that each sample within the array comprises a "component-in-common" (e.g., see claim 22 wherein the "compound-of-interest" is the "component-in-common" because "each sample" contains such a compound-of-interest). In addition, Levinson et al. disclose that one or more additional components can vary in identity and/or ration of volumes (e.g., see claim 26, "wherein one or more of the processed samples differ from one or more other processed samples with respect to at least one of ... amount or concentration of the compound-of-interest ... the identity of one or more of the components"). In addition, Levinson et al. disclose that the samples are in separate sites or in separate wells of the array (e.g., see abstract and/or drawing showing separate wells of microtiter plate). Levinson et al. also disclose the use of at least 1000 different samples (e.g., see claim 37, "wherein at least about 1000 samples are processed in parallel"). Furthermore, Levinson et al. disclose the use of

"automated robotics" to prepare the sample under software control (e.g., see Levinson et al., specification, section 6.1). Finally, Levinson et al. also disclose "testing" each sample for a property to generate a data set and "analyzing" said data set to measure or detect an interaction between components of the sample formulations (e.g., see Levinson et al., specification, section 6.1, "These systems [robotic analysis] are connected to computers for analysis of the data using appropriate software and data sets"; see also last paragraph in section 6.1, "The presence of solid-forms is then determined, for example, by optical detection, and the solvent removed by filtration or evaporation. The crystal properties, such as polymorph or habit can then determined using techniques such as Raman, melting point, x-ray diffraction, etc., with the results of the analysis being analyzed using an appropriate data processing system"; see also section 6.4.4., "Image-analysis techniques ... allow one to obtain information about a sample ... that would aid in elucidating the structure, property, or behavior of a material, for example, crystal habit). For claim 155, Levinson et al. further disclose the use of one or more additional pharmaceutical components and one or more additional excipients components (e.g., see Summary of Invention; see also section 4.3, "The term "compound-of-interest" means ... pharmaceuticals"; see also section 4.3.2; see also section 4.4., "Examples of components include, but are not limited to, excipients"; see also section 4.4.1; see also claim 28, "adding one or more additional components"; see also claim 27, "The method of claim 22, wherein one or more of the components is an excipient ... a pharmaceutical").

For ***claim 139***, Levinson et al. disclose adding an active component-in-common (e.g., see claim 33, "The method of claim 22, wherein the compound-of-interest [i.e.,

common to all samples] is a an active component of a consumer formulation, or an active component of an industrial formulations").

For ***claims 140, 141, 155 and 158***, Levinson et al. disclose adding a component-in-common that is a pharmaceutical (e.g., see claim 33, "wherein the compound-of-interest [i.e., common to all samples] is a pharmaceutical"). In addition, Levinson et al. disclose a pharmaceutical that is a therapeutic (e.g., section 4.4.4.3, "Discovery of additives that direct formation of one polymorph over another or promote conversion of a less stable polymorph into the more stable form are of considerable importance, for example, in the pharmaceutical industry, where certain polymorphs of a given pharmaceutical are more therapeutically beneficial than other forms")

For ***claims 144, 149, 160 and 165***, Levinson et al. disclose adding the component-in-common in a liquid form (e.g., see section 4.8, "According to the invention described herein, the "physical state" of a component or a compound-of-interest [i.e., common to all samples] is initially defined by whether the component is a liquid or a solid").

For ***claim 145 and 161***, Levinson et al. disclose adding less than 100 μg of the component-in-common (e.g., see claim 24, "wherein the amount of the compound-of-interest in each sample is less than about 100 micrograms").

For ***claims 146 and 162***, Levinson et al. disclose adding less than 100 ng of the component-in-common (e.g., see claim 25, "wherein the amount of the compound-of-interest in each sample is less than about 100 nanograms").

For ***claims 147 and 163***, Levinson et al. disclose adding a total volume between 150 and 200 volume between 150 and 200 µl (e.g., see section 4.2, "Preferably, the sample has a total volume of 100-250 ul").

For ***claims 150 and 166***, Levinson et al. disclose testing at a rate greater than or equal to 1000 formulations per day (e.g., see section 6, "applicants have developed high-throughput methods to produce and screen hundreds, thousands, to hundreds of thousands of samples per day").

For ***claims 151-154, 167-170***, Levinson et al. disclose analyzing the data to arrive at optimized formulations (e.g., see Summary of Invention, "Thus, one would add simulated gastric fluid if the application if to optimize the dissolution of drug substance in oral dosage forms"; see also section 6, "These methods are useful to optimize, select, and discover new, solid-forms having enhanced properties"; see also section 6.1, "These systems are connected to computers for analysis of the data using appropriate software and data sets"). Please note that the limitation drawn to "the ability of scientific personnel" to perform various functions is not given any patentable weight as it represents "intended use" (e.g., see claims 152-154 and 168-170; see also MPEP § 2144).

For ***claims 171 and 172***, Levinson et al. disclose, for example, acidulents (e.g., see section 4.3.2).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 136, 139-141, 144-147, 149-151, 155, 158, 160-163 and 165-168, 171-172 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ferris (US Patent No. 4,808,705) (Date of Patent is **February 28, 1989**) and Mere et al. (Mere, L.; Bennnett, T.; Coassin, P.; England, P.; Hamman, B.; Rink, T.; Zimmerman, S.; Negulescu, P. "Miniaturized FRET assays and microfluidics: key components for ultra-high-throughput screening" **August 1999** *DDT*, 4(8), 363-369) and Promega Inc. (Promega Inc. "CellTiter 96 AQueous One Solution Cell Proliferation Assay" **1996** *Neural Notes*, 11(3), 15).

For ***claims 136 and 155***, Ferris (see entire document) teach methods for, "... screening for compounds [e.g., additional components like excipients] that stabilize RTA [e.g., component-in-common] in solution, and are therefore considered to be suitable candidate stabilizers for RTA-immunoconjugate preparations" (e.g., see Ferris, Summary

of Invention), which reason on the claimed invention. For example, Ferris teaches preparing an "array" of samples (e.g., see column 9-10, Cytotoxicity Assay section, especially lines 28 and 35 wherein a "96-well" array is disclosed). In addition, Ferris teaches that each sample in the array comprises a component-in-common (e.g., each sample contains the RTA or RTA-immunoconjugate (e.g., see Cytotoxicity Assay section, lines 9-11, "A colorimetric cytotoxicity assay was used to test the biological activity of the RTA-immunoconjugates that had been lyophilized in the stabilized pharmaceutical compositions of this invention, and then reconstituted and subjected to agitation"; see also column 2, lines 41-44, "One aspect of the instant invention concerns highly stable compositions comprising RTA dissolved in an inert carrier medium comprising a stabilizer selected by the screening processes described herein"; see also Thermal Stability Assay Screening Method section, especially column 6, lines 5-45, "A heat denaturation assay was developed to screen a large number of reagents for their ability to stabilize RTA and RTA-immunoconjugates ... Comparisons can be made between absorbance readings of RTA preparations [e.g., component-in-common] with various concentrations of the candidate stabilizer [e.g., additional components] to optimize the effective concentration thereof"). In addition, Ferris teach that one or more additional components can be added and that these additional components can vary in identity and/or volume (e.g., see column 6, lines 5-45, "A heat denaturation assay was developed to screen a large number of reagents for their ability to stabilize RTA and RTA-immunoconjugates ... Comparisons can be made between absorbance readings of RTA preparations with various concentrations of the candidate stabilizer [i.e., additional

component] to optimize the effective concentration thereof [i.e., volume ratio can vary] ... Candidate stabilizer compounds can be selected from any reagent class [i.e., identity can vary]"; see also column 7, lines 6-9, "comparing the absorbance curve of step (a) and that of step (c) to determine the effectiveness of the candidate stabilizer in preventing aggregation and precipitation of the RTA"; see also column 6, lines 39-45, "Candidate stabilizer compounds can be selected from any reagent class, but preferably from ... excipients"). Ferris also teach the use of testing each sample for a property to generate a data set and analyzing said data (e.g., see column 6 wherein the "thermal stability" is tested as a property; see also figures where this information is used generate data sets that is shown graphically; see also column 7, lines 5-9 wherein the absorbance curve data sets were used to "select" the optimal candidate stabilizers, "comparing the absorbance cure of step (a) and that of step (c) to determine the effectiveness of the candidate stabilizer"; see also column 9, Cytotoxicity assay wherein the sample are tested for their ability to kill MCF-7 cells and subsequently analyzed to pick the formulations that exhibit the optimal cytotoxicity). Thus, Ferris teach a method for screening pharmaceutical formulations of biologically active RTA conjugates including the use of various excipients for obtaining "optimal" stability and/or retention of biological activity using automated screening procedures with 96 well microtiter plates.

For ***claims 139-141, 158***, Ferris discloses the active RTA pharmaceutical conjugates (e.g., see abstract, "Highly stable pharmaceutical compositions ... comprising a therapeutically effective [i.e., active] amount of an RTA-immunoconjugate").

For ***claims 144, 149, 160, 165***, Ferris also discloses a Sodium phosphate/PBS inert carrier medium as a liquid component-in-common (e.g., column 5, lines 45-64, "Sodium phosphate is another preferred inert carrier medium, preferably at the same molarity range as indicated for PBS").

For ***claims 145-147, 161-162, 163***, Ferris discloses a wide range of amounts (e.g., see paragraph bridging columns 5-6, "The concentration of the RTA-immunoconjugates in the pharmaceutical compositions of this invention are preferably from about 0.002 mg/ml to about 20 mg/ml, more preferably from about 0.01 to 10 mg/ml, still more preferably from about 0.05 to 4 mg/ml, and most preferably about 2 mg/ml"; see also Example 2, "Five hundred ul of the immunoconjugate (1 mg) was mixed with each of 5 samples of 25% HSA in the following volumes: 40 ul, 80 ul, 120 ul, 160 ul and 200 ul").

For ***claims 151 and 167***, Ferris teach the "optimization" of the samples by analyzing the data (e.g., see e.g., see column 6, lines 5-45, "A heat denaturation assay was developed to screen a large number of reagents for their ability to stabilize RTA and RTA-immunoconjugates ... Comparisons can be made between absorbance readings of RTA preparations [i.e., a data set] with various concentrations of the candidate stabilizer [i.e., another data set] to optimize the effective concentration thereof).

For ***claims 171-172***, Ferris teach buffering components such as PBS (e.g., see Example 1).

The prior art teachings of Ferris differ from the claimed invention as follows:

For ***claim 136 and 155***, Ferris is deficient in that they do not specifically teach the use of automated robotics to help speed up the screening process nor does Ferris teach the use of 1000 different samples.

For ***claims 145-146, 161-162***, Ferris does not disclose an array with less than 100 ng of the component-in-common.

For ***claims 150, 155, 166***, Ferris does not disclose 1000 formulations per day.

However, Mere et al. and Promega Inc. teach the following limitations that are deficient in Ferris:

For ***claim 136 and 155***, the combined teachings of Mere et al. (see entire document) and Promega Inc. (see entire document) show that cell-based assays such as the tetrazolium cell-based cytotoxicity assay disclosed by Ferris can be performed in a high throughput fashion using, for example, the 3456-well NanoWell assay plates that includes robotics as disclosed by Mere et al. (e.g., see Mere et al., figure 1; see especially the "reagent dispensing robot") and the improved CellTiter96 AQueous One Solution Cell Proliferation Assay disclosed by Promega Inc. that is commercially available in a 5,000 assay size (e.g., see Promega Inc., page 15).

For ***claims 145-146, 161-162***, the combined teachings of Mere et al. and Promega Inc. show that the total volume of the samples (and thus the total amount of the component-in-common) can be reduced by a factor of 200 (e.g., see Mere et al., page 263, column 1, paragraph 1, "Reduction of assay volume from 50-200 μl per well to 1-2 μl per well requires a comprehensive approach ...").

For ***claim 150, 155 and 166***, the combined teachings of Mere et al. and Promega teach >1000 samples per day (e.g., see abstract wherein the 3456-well plate is used; see also page 363, column 2, "One primary purpose ... is the automated screening of over 100,000 compounds ... per day").

It would have been obvious to one skilled in the art at the time the invention was made to scale up the formulation production and screening as taught by Ferris with the methods and/or apparatus disclosed by the combined teachings of Mere et al. and Promega Inc. because Mere et al., for example, explicitly state that their 3456-well high throughput screening techniques can be applied to standard cell-based assays that would include the standardized cell-based cytotoxicity assays as disclosed by Ferris and Promega. Furthermore, one of ordinary skill in the art would have been motivated to use the high throughput screening techniques and/or apparatus because Mere et al. explicitly state, "the assay technologies and instrumentation should be useful for significant enhancement of distributed, research laboratory based screening programs", which would encompass the screening program disclosed by Ferris. Mere et al. also state that their methodology and instrumentation provides "rapid" screening with "smaller" sample volumes, which would enable a larger number of the formulations disclosed by Ferris to be screened in a shorter period of time (e.g., see Mere et al., page 366, column 2, last paragraph, "One important advantage of miniaturization is conservation or reagents, including the ability to use only small quantities of cultured cells"). In addition, a person of skill in the art would have been motivated to use the CellTiter 96 assay disclosed by Promega Inc. because according to Promega Inc. the assays can be performed in 96 well

plates in a fast, convenient, flexible way when compared to the standard tetrazolium assays disclosed by Ferris (e.g., see Promega Inc., Table 1). Finally, a person of skill in the art would reasonably have expected to be successful because Mere et al. state that their instrumentation and methods are specifically designed for cell-based assays, which would encompass the cell-based assays disclosed by Ferris (e.g., see Mere et al., page 365, column 1, last paragraph, "The Reagent Dispensing Robot (RDR) is designed for precise, high-speed dispensing of assay reagents, including cell suspensions, into high-density plates"). Furthermore, Mere et al. state that their system is compatible with 96-, 384- and 3456-well plate formats and fluorescent plate readers, which would include the 96-well plate/reader format disclosed by Ferris and Promega Inc.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 36, 139-141, 144-147, 149-155, 158, 160-163 and 165-172 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 180-304 of copending Application No. 09/756,092 (Pub. No.: US

2002/0048610 A1) (referred to herein as '092) in view of Levinson et al. (WO 01/51919 A2) and/or Merrittt (Merrittt, A. T. "Uptake of new technology in lead optimization for drug discovery" **1998**, *DDT*, 3(11), 505-510). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986).

Here, the '092 application discloses **[1]** the preparation and use of an "array" (e.g., compare claims 136, 145-147, 149, 155 and 160-163 of the present application to claims 180, 184-186, 194, 198, 202-204, 212, 220 of '092 wherein the use of an "array" is disclosed), **[2]** a component-in-common (e.g., compare claims 136, 139-141, 144-146, 155 and 158, 160-161 of the present application wherein a "component-in-common" is disclosed to claims 180, 198, 200, 201, 228-231, 234, 236, 255, 256 of '092 wherein a "small molecule pharmaceutical" that is contained in "each" sample and thus represents a "component-in-common" is disclosed), **[3]** one or more additional components (e.g., compare claims 136 and 155 of the present application to claims 180, 207, 215 and 223 of '092 wherein "one or more additional components" are disclosed), **[4]** varying the identity of said additional components and/or the ratio of the volume of the component-in-common to the volume of the one or more additional components (e.g., compare claims 136 and 155 of the present application to claims 180, 235, 246, 302 and 303 wherein the "additional component" disclosed by the present application is the "one or more solvent, acid or base" disclosed in '092), **[5]** the use of separate sample wells (e.g., compare

claims 136 and 155 of the present application to claim 180 of '092), **[6]** at least 1000 different samples (e.g., compare claims 136, 150, 155 and 166 of the present invention to claim 185 of '092), **[7]** the use of "automated robotics" to prepare samples under "software" control (e.g., compare claims 136 and 155 of the present application disclosing an "automated robotics system" to claims 180, 186 and 302-304 disclosing an "automated distribution mechanism" or an "automated dispensing mechanism") wherein said distribution/dispensing mechanism is defined to include "robotics" (e.g., see '092 specification, section 6.1; see also MPEP § 804, "The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. *In re Boylan*, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970)"), **[8]** testing each sample for a property (e.g., compare claims 136, 150, 155 and 165 of the present application disclosing "testing" each sample for a property to claims 180 "measuring" each sample i.e., testing/measuring are used interchangeably) and **[9]** analyzing the data set to measure or detect an interaction between components of the sample formulation (e.g., compare claims 136 and 155 of the present application to claims 180 and 302-304 wherein "informatics" is used to measure or detect an interaction between components of the sample formulation and "group" said samples based on this measurement and/or detection into "families"; see also '092 specification, section 6.5.1, "The collected data can be analyzed using informatics. Informatics protocols enable high-throughput analysis of spectroscopic, diffractometric, and thermal analyses and thereby enable identification of crystal forms that

belong to the same polymorph family. These informatics tools facilitate identification of conditions that define occurrence domains (i.e., thermodynamic and kinetic parameters) that will give rise to a specific crystal form"; see also MPEP § 804, "The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. *In re Boylan*, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970)").

The methods disclosed by '092 differ from the claimed method by failing to recite the use of "robotics" as an automation tool for use in high throughput screening. However, Levinson et al. and/or Merrittt disclose the use of "robotics" in high throughput screening (e.g., see Levinson et al., abstract; see also section 6.1 wherein the use of robotics is disclosed; see also Merrittt, page 505, column 2, last paragraph). Thus, it would have been obvious to "robotic" automation because both Levinson et al. and Merrittt disclose the use of robotics for various pharmaceutical applications including the use of such automation to prepare samples with a "component-in-common" such as a small molecule pharmaceutical and also the addition of components such as excipients (e.g., see Levinson et al., abstract, see also claims). One having ordinary skill in the art would have been motivated to make such a modification because Levinson et al. state that robotics is a preferred embodiment (e.g., see Levinson et al., section 6.1; see also Merrittt, page 510, column 1, last paragraph stating that such robots have "revolutionized" lead optimization). Finally, a person of skill in the art would have reasonably expected to be successful because according to Levinson et al., "Such material handling technologies and robotics are well known

to those skilled in the art" (e.g., see section 6.1; see also Merit, "highly technical and computer controlled equipment is now commonplace in laboratories").

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 36, 139-141, 144-147, 149-155, 158, 160-163 and 165-172 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 170-178 (especially claims 174-178) of copending Application No. 10/372,524 (Pub. No.: US 2003/0162226 A1) (referred to herein as '524) in view of Levinson et al. (WO 01/51919 A2) and/or Merrittt (Merrittt, A. T. "Uptake of new technology in lead optimization for drug discovery" **1998**, *DDT*, 3(11), 505-510). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986).

Here, the '524 application discloses **[1]** the preparation and use of an "array" (e.g., compare claims 136, 145-147, 149, 155 and 160-163 of the present application to claims 170-174 and 176 of '524 wherein the use of an "array" is disclosed), **[2]** a component-in-common (e.g., compare claims 136, 139-141, 144-146, 155 and 158, 160-161 of the present application wherein a "component-in-common" is disclosed to claims 170-175 of '524 wherein a "compound-of-interest" that is contained in "each" sample and thus represents a "component-in-

common" is disclosed), **[3]** one or more additional components (e.g., compare claims 136 and 155 of the present application to claims 170 and 174-176 of '524 wherein "one or more additional components" are disclosed), **[4]** varying the identity of said additional components and/or the ratio of the volume of the component-in-common to the volume of the one or more additional components (e.g., compare claims 136 and 155 of the present application to claims 170 and 174-176 wherein the "the identity of one or more of the components" is varied) and **[5]** the use of separate sample wells (e.g., compare claims 136 and 155 of the present application to claim 180 of '524).

The methods disclosed by '524 differ from the claimed method by failing to recite **[1]** the use of "robotics" as an automation tool for use in high throughput screening, **[2]** use of "1000" samples and **[3]** the use of data sets to measure and detect interactions. However, Levinson et al. and/or Merrittt disclose the use of "robotics" in high throughput screening (e.g., see Levinson et al., abstract; see also section 6.1 wherein the use of robotics is disclosed; see also Merrittt, page 505, column 2, last paragraph). Levinson et al. and Merrittt also disclose the use of at least 1000 different samples (e.g., see Levinson et al., claim 37, "wherein at least about 1000 samples are processed in parallel"). In addition, Levinson et al. and Merritt disclose "testing" each sample for a property to generate a data set and "analyzing" said data set to measure or detect an interaction between components of the sample formulations (e.g., see Levinson et al., specification, section 6.1, "These systems [robotic analysis] are connected to computers for analysis of the data using appropriate software and data sets"; see also last paragraph in section 6.1, "The presence of solid-forms is then determined, for example, by optical detection, and the solvent removed by filtration or evaporation. The crystal properties, such as polymorph or habit

can then determined using techniques such as Raman, melting point, x-ray diffraction,etc., with the results of the analysis being analyzed using an appropriate data processing system"; see also section 6.4.4., "Image-analysis techniques ... allow one to obtain information about a sample ... that would aid in elucidating the structure, property, or behavior of a material, for example, crystal habit).. Thus, it would have been obvious to "robotic" automation because both Levinson et al. and Merrittt disclose the use of robotics for various pharmaceutical applications including the use of such automation to prepare samples with a "component-in-common" such as a small molecule pharmaceutical and also the addition of components such as excipients (e.g., see Levinson et al., abstract, see also claims). One having ordinary skill in the art would have been motivated to make such a modification because Levinson et al. state that robotics is a preferred embodiment (e.g., see Levinson et al., section 6.1; see also Merrittt, page 510, column 1, last paragraph stating that such robots have "revolutionized" lead optimization). Finally, a person of skill in the art would have reasonably expected to be successful because according to Levinson et al., "Such material handling technologies and robotics are well known to those skilled in the art" (e.g., see section 6.1; see also Merit, "highly technical and computer controlled equipment is now commonplace in laboratories").

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
March 15, 2005